PATENT
Attorney Docket No: STEM1110-5

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Twardzik et al.	Art Unit:	Unassigned
Application No.	Unassigned		
Parent Application No.:	09/641,587	Examiner:	Unassigned
Filed:	January 15, 2002		
Title:	TGF-α POLYPEPTIDES, FUNCTIONAL FRAGMENTS AND METHODS OF USE THEREFOR		

Commissioner for Patents
Washington D.C., 20231

Sir:

PRELIMINARY AMENDMENT

Prior to the examination of the present application, please amend the application as follows:

IN THE SPECIFICATION:

Please delete the paragraph on page 1, under the heading "CROSS REFERENCE TO RELATED APPLICATIONS" and insert the following replacement paragraph:

-- **[0001]** This application is a continuation of 09/641,587, filed August 17, 2000, now abandoned which is a continuation-in-part of U.S. Application 09/492,935, filed January 27, 2000, which is a continuation-in-part of U.S. Application 09/378,567, filed August 19, 1999, now abandoned the disclosures of which are herein incorporated by reference in their entirety.--

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with exogenous antigen. The T cell progenitor cells appear to be double null and thus naive. Accordingly, the T cell progenitor cell response to TGF-α and TGF-α mimetics provides the utility for such compounds to provide a strong mucosal immunity response and usefulness as a mucosal vaccine and as a universal stem cell adjuvant.

During a course of therapy organs may be targeted by specific chemical agents, however, organ damage can be a side effect. In United States patent application 09/299,473 filed 26 April 1999 (now abandoned) (the disclosure of which is incorporated by reference herein), the effects of increasing hematopoiesis based upon hematopoietic injury from cytotoxic cancer therapy is described. These data can be further expanded to organ damage caused by chemicals known to cause specific organ damage. As shown below, gentamycin is an antibiotic known to cause kidney damage as a dose-limiting side effect. Histological data shows that the kidney damage seen in glomeruli of kidneys is alleviated by concurrent and subsequent administration of a TGF-α polypeptide (in this case a TGF-α57 polypeptide was used). Kidney damage can also occur following exposure to cancer chemotherapeutic agent, such as cis platinum, or gentamycin or the toxin from *E. coli* 0H1:37 from undercooked contaminated meats. Intestinal damage can occur form many cancer chemotherapeutic agents, cholera toxin, and the like. Lungs can be damaged by the anti-cancer agent bleomycin. Accordingly, administration of a TGF-α polypeptide, fragments, or mimetic before, during and following exposure to an organ toxic agent can prevent organ damage.

In addition, administration of a TGF-α polypeptide, fragments, and mimetic to regenerate damaged tissue, for example, in kidney, an organ sensitive to such damage, is also disclosed herein. In an *in vivo* experiment, mice were administered 10 mg/kg of Cis-platinum as a single ip injection and treated mice administered 10 μg/kg a human TGF-α57 (R&D Systems, Minneapolis, MN). TGF-α57 was administered just before CP and in two additional doses after, by ip administration for a general systemic effect. Several organs or tissues were collected from the animals sacrificed 4 days after CP dose (or saline for no TGFα57) and tissues were examined histologically.